## REMARKS

Applicants request entry of the amendments and remarks submitted herein. Claim 1 has been amended herein, and claim 7 has been cancelled without prejudice to continued prosecution. Support for the amendment to claim 1 can be found in the application as filed, for example, in the specification at paragraph [0038]. Claim 8, which stands withdrawn, has been amended to correct the dependency in the event of rejoinder. No new matter has been introduced by these amendments.

Claims 1, 2, 4, and 5 are pending, and claims 6 and 8 are withdrawn. Reconsideration of the pending application is respectfully requested.

### Rejection under 35 U.S.C. §102(e)

Claims 1, 2 and 7 stand rejected under 35 U.S.C. §102(e) as anticipated by Velculescu *et al.* (US2007/003185). The Examiner asserts that Velculescu discloses a 10-mer oligonucleotide that "may be comprised in an array and is 100% complementary within the region recited in the instant claims." Claim 7 has been cancelled and thus the rejection applied to this claim is now moot.

Without acquiescing to the Examiner's rejection and solely for the purpose of furthering prosecution, claim 1 has been amended to recite an antisense oligonucleotide consisting essentially of 12 to 40 nucleotides. Thus, the size range of the antisense oligonucleotide of the claims falls outside the size of the oligonucleotides disclosed in the reference. Applicants therefore respectfully request that the rejection of claims 1 and 2 under 35 U.S.C. §102(e) be withdrawn.

### Rejection under 35 U.S.C. §103

Claims 1, 2, 4 and 7 stand rejected under 35 U.S.C. §103 as obvious over Philipp (*J.Biol.Chem.* (2000) 275: 23965-23972) in view of Liang *et al.*, (WO 02/24950) and Noonberg *et al.*, (U.S. Patent No. 5, 642,803). Although the Examiner states: "Philipp *et al.* have therefore taught to use antisense technology to inhibit TRPC4" (Office Action at page 4), the

Examiner also clearly recognizes that Philipp does not disclose the particular size range and targeted region required by the present claims.

Philipp discloses inhibiting TRPC4 using a vector that expressed the *complete* coding sequence, a segment of more than 2900 nucleotides, of bovine TRP4 in an antisense orientation. (See Philipp *et al.*, p. 23966, left hand column). On the other hand, the claimed antisense oligonucleotide is 12-40 nucleotides in length and specifically hybridizes to a region defined by nucleotides 43 through 86 of SEQ ID NO:1, *i.e.*, rat TRPC4. As the Examiner acknowledged, Philipp "does not teach the recited target region of the instant invention." (Office Action at page 5). Indeed, Philipp's failure to disclose the size range and specifically-claimed accessible region forced the Examiner to search for and apply Liang and Noonberg. (Office Action at page 4).

Neither Liang nor Noonberg discloses or even mentions TRPC4 sequences, and, of course, neither reference discloses the particularly claimed accessible region (*i.e.*, nucleotides 43 through 86 of SEQ ID NO:1). Liang discloses general methods for identifying regions within a mRNA sequence that are accessible to hybridization by antisense molecules, and Noonberg discloses methods for the efficient intracellular delivery of oligonucleotides using novel constructs that utilize an RNA polymerase III promoter for intracellular expression of the antisense oligonucleotide. Noonberg is cited simply for it's disclosure regarding the optimal length of antisense oligonucleotides (i.e., 10 to 60 nucleotides in length).

Applicants note that the mere use of a method for identifying an accessible region within an mRNA, whether that of Liang or the more traditional trial-and-error approach, does not make obvious the specifically claimed accessible region within the specifically claimed TRPC4 sequence. At the time the application was filed, identification of functional antisense oligonucleotide sequences, *i.e.*, antisense molecules that modulate expression of the corresponding gene, was unpredictable at best, and generally involved random selection of the region to which the antisense oligonucleotide will hybridize followed by empirical testing of each antisense oligonucleotide. According to Liang, only a small proportion (2-10%) of antisense oligonucleotides actually exhibited sequence-specific inhibition of expression (see, for example, page 2, lines 5-7).

One of skill in the art, merely from reading the cited references, simply would have no way of knowing that a region defined by nucleotides 43 through 86 of SEQ ID NO:1 would be

accessible to antisense oligonucleotide binding and that oligonucleotides that specifically hybridize to that region would inhibit the production of TRPC4. In view of the remarks herein, applicants respectfully request that the rejection of claims 1, 2, 4 under 35 U.S.C. §103 be withdrawn.

Request for Rejoinder

Claims 6 and 8 were withdrawn as directed to a non-elected invention following the Restriction Requirement of November 22, 2006 and Applicants' election of May 22, 2007. Since claim 1 should be allowable in view of the amendments and remarks herein, Applicants respectfully request that claims 6 and 8 be rejoined and allowed pursuant to MPEP §821.04(b).

## CONCLUSION

For at least the foregoing reasons, Applicants submit that claims 1, 2, 4, 5, 6 and 8 are in condition for allowance, which action is respectfully requested. The Examiner is invited to call the undersigned if such will advance prosecution of this application. Please apply the fee for the accompanying Petition for Extension of Time and any other charges or credits to Deposit Account No. 06-1050.

Respectfully submitted,

/September 22, 2008/

Date:_____

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